DIP #621

USMLE Step 2, 3 Rapid Review Series 129

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- **Dr Mohammed Zaki**
https://chat.whatsapp.com/L6dShASc3f97cwHZgCD6Xo

- So what if they give you a question about a?
- We're told that we have this **2-year-old child** and this child for the last week has had **very high fevers, very, very high fevers**.
- They tell you that this child has become more and more **lethargic**, and then they tell you that on the child's skin you see a lot of **petechiae and purpura**.
- And they give you a bunch of labs and you notice that this child's **white count is pretty high**.
- And with that high white count, you see a lot of **lymphocytes**.
- You see the **platelet count is extremely low**, right?
- And then they tell you that the child has **hepatomegaly**, this also has **splenomegaly**, and that the child has a **diffuse lymphadenopathy**.
- When you see this, then they then ask without treatment, without treatment, what may happen to this child within the next few weeks.
- I really hope you're taking the answer that says **death**.

- So what does this child have?
- So this child has **ALL**, right.
- This child has **ALL**.
- **ALL** is really bad, right.
- And it's one of the more common **pediatric hematologic malignancies**, right.

- And I think there is something I want to emphasize here.
- That can really draw some knowledge out that can really help you on your exams.
- The thing is, many people do not believe this, but these are **acute leukemias**.
- You can **die from them quickly**.
- In my experience, they tend to have good treatment, like if you treat them you recover from them.
- But if you don't treat them from when your symptoms begin to death, it's usually pretty short, pretty short, sometimes you can be **dead within a couple of weeks**, right?

- So this child has **ALL**.
- So how does **ALL** classically present on the **USMLE exams**?
- **ALL is going to present on the USMLE exams with the following:**
    - #1 is going to be in a **little child**, right, he's going to be a little child on your test, right.
    - #2, they're gonna have **diffuse lymphadenopathy**.
    - Their **spleens may also be big**.
    - Their **livers may be big**, and typically they will have a **leukocytosis** that is predominantly **lymphocytosis**, right?
    - **Predominantly lymphocytosis**.
    - And you may notice that there are **other cell lines**.
    - There are platelets, there are red cells may be reduced.
    - In fact, typically you may notice that they may have antecedents of low levels of those other blood elements, right, like for example.
    - You see me talking about these **petechiae and purpura** on this child's skin.
    - Those are signs of **thrombocytopenia**, right.
- So **ALL has to be treated**.
- If they don't really quickly, the child is going to **die**, right.

- So these **acute leukemias**, they tend to have pretty sudden presentations, right?
- Like, even **AML in adults**, AML in adults is something that has to be treated and treated fast.
- If you don't treat fast, the adult may not survive.

- That's something that's very important to know for your exams, right?
- Like, for example, many of you are probably familiar with **acute promyelocytic leukemia** with those **15;17 translocations**.
- Typically, they can present with the **DIC presentation**, right.
- Because those **blast cells** in acute leukemias, they can make **tissue factor**, right.
- And that can trigger the **coagulation cascade**, right?
- So those things have to be treated quickly.
- If you don't treat them quickly, the person may not make it, right.
- If you don't treat them quickly, the person may not make.

- And then **ALL**, what are some other high-yield things you want to make sure about **ALL**?
- **Some other high-yield things about ALL:**
    - Number one, if a child has **ALL**, don't be afraid to give them **chemotherapy**.
    - You're going to give them **chemo**.
    - But don't be afraid as well to potentially give them... What am I trying to get at here?
    - Don't be afraid to give them the **treatment quickly**.
    - I think that's what I'm trying to emphasize here.
    - Don't be afraid to give them the **treatment quickly** because the thing is...
- Sometimes they can make it into an **ethics question**.
- And with that ethics question you notice that oh the parents want to try something like some kind of **alternative medicine therapy**.
- The thing is, that's not the way to go, right?
- You have to **override those parents** because that kid is going to **die quick**, right.
- So in those circumstances you need to **override the parents**.
- Either get the **courts** to come and decide in your favor, right?
- But that child needs to get **treated**, right.
- Any other alternative medical whatever that the parents want to try, that's not gonna fly on the **USMLE exams**, right.

- And then don't forget that, **ALL**.
- People that have **Down syndrome**, people that have **Down syndrome**, **Down syndrome** actually has a pretty solid association with **ALL**, right.
- Don't forget that **association between Down syndrome and ALL**, right.
- Let's go ahead and move on to something else.

- So what if they give you a question about a patient and they tell you that this patient is a **35-year-old African American male**?
- And he comes to the physician because he's noticed at a **health fair** that his **blood pressure** has been elevated.
- And we're told that at the health fair, his blood pressure was found to be like **165/105**.
- Over the last few days, he has been checking his blood pressure at home with an **over-the-counter purchased blood pressure monitor**, and they give you a list of his blood pressures, right.
- The **USMLE** is kind of cheesy and corny like this.

- They'll give you a list of **home blood pressures**, measured over like a week or two weeks or something.
- And you notice that all those pressures are high.
- They're still like in the **160s systolic**, some in the **170s**, and many in the **100s diastolic**, right.
- And then they tell you that the blood pressure and these results are also **confirmed in the office**.
- And then you are asked: **which of the following is the most appropriate?**
- They give you some other labs, you notice that **creatinine is completely fine**, his **A1C is totally good**.
- And then they ask you which of the following is the **most appropriate next best step in management**.
- And I really hope that you're picking some answer that relates to either a **thiazide diuretic** or a **calcium channel blocker**, a **dihydropyridine calcium channel blocker**, right.

- The thing is, many people can screw this up on the exams.
- So I want to kind of spend a little bit of time talking about this, right.
- So if you notice this vignette I gave was an **African American**, right?
- The thing is, when people are **African Americans** and they have **high blood pressure**, you have to start them on a **thiazide** or a **dihydropyridine calcium channel blocker** as **first-line**.

- I'm going to say that again:
- When a person is an **African American** and they have **high blood pressure**, if you're starting them on an **antihypertensive**, the **first-line antihypertensive** in this population is a **dihydropyridine calcium channel blocker** like **amlodipine** or a **thiazide diuretic** like **hydrochlorothiazide, chlorthalidone**, and things like that.
- **ACE inhibitors and ARBs** are **not indicated as first-line** for **hypertension in African Americans** if they don't have a **secondary need for it**.
- I'm going to say that again:
- **ACE inhibitors and ARBs** are **not indicated as first-line** for the management of **hypertension in African Americans** if they do not have a **secondary need for it**.

- So what do I mean by a **secondary need**?
- A secondary need is going to be something like **diabetes**, right?
- Because remember, **ACE inhibitors and ARBs** are **renal protective** in a person that has **diabetes**, right?
- Because remember, they **dilate your efferent arteriole**.
- When they dilate those efferent arterioles, they're going to **reduce the hydrostatic pressures within your glomerular capillaries**, right.
- So that's going to **reduce intraglomerular hypertension**.
- That's going to prevent **hyperfiltration injury**, because when you have **diabetes**, you have **non-enzymatic glycosylation** of your different arterioles.
- When that happens, that's going to basically cause a **constriction of your efferent arterioles**.
- And when that happens, you're going to raise the **blood pressures within your glomeruli**, and that's going to raise your **GFR transiently**, right — until your kidneys basically die, right.

- And that rising GFR can cause injury, known as **hyperfiltration injury**.
- Too much filtration can **damage the glomeruli over time**, right.
- You have all those **Kimmelstiel-Wilson nodules** and all those problems, right.
- So **ACE inhibitors and ARBs** help with that process by **dilating the efferent arteriole**.
- That's going to **pull blood away from the glomerular capillaries**.
- That's going to **reduce the hydrostatic pressure within those glomerular capillaries**.
- And that's going to be **very, very helpful**, right.

- So now, if you have **diabetes**, right, or let's say you have **heart failure** — because remember **ACE inhibitors** improve survival in heart failure — then yes, in those circumstances you can start an **ACE inhibitor** or an **ARB** for **high blood pressure in African Americans**.
- But if they don't have those secondary indications, you really should note on your exams this is one of those things.
- The resources don't cover it, but it's actually very, very **high-yield** to know for your tests.
- The thing is, there have been some studies that show **ACE inhibitors and ARBs** are **not as effective in African Americans** for high blood pressure compared to other populations, right?
- So something you want to keep at the back of your mind for your exams, right.

- And then what are some **unique quirks** you want to know about some of these **antihypertensives**, right?
- I just kind of want to hit on a few that are commonly tested on the **USMLE exams**, right.

Pregnancy & Antihypertensives

- So remember, if a person is **pregnant**, you want to be aware of the **teratogenic antihypertensives**.
- What are those teratogenic antihypertensives?
    - **ACE inhibitors** and **ARBs**.
    - They can cause a lot of **renal problems in the fetus**.
    - That is not ideal — you don't want that for a fetus, right.
- So typically on the **USMLE exams**, what are you going to do for those women?
    - You're going to give them something like **hydralazine**, or **methyldopa**, or **labetalol**, or **nifedipine**.
    - So those are the drugs you're going to use to control blood pressure in **pregnancy**, right.
- There's this mnemonic: **Hypertensive Moms Love Nifedipine**.
    - **Hydralazine**
    - **Methyldopa**
    - **Labetalol**
    - **Nifedipine**
- You can use any of those, and those drugs also happen to be the ones you can use to manage **hypertensive emergencies in pregnancy**, like **HELLP syndrome**, or **preeclampsia**, or things of that nature, right.
- So that's something to keep at the back of your mind for your exams.

Hypertension with Comorbidities

- If a person has **high blood pressure** and the person has **BPH**, right?
    - In that case you want to give those people an **alpha-1 blocker**, right?
    - It's gonna kill those two birds.
    - It's gonna help them with their **high blood pressure**.
    - But it's also gonna help **open up the bladder neck**, and that's gonna help them **pee better**, right.

Hypertension and Nephrolithiasis

- And then what if a person has a history of **nephrolithiasis**?
- What kind of antihypertensive would you recommend for these people?
- I hope you're saying a **thiazide diuretic**.
- Why?
    - Because **thiazides** actually cause you to reabsorb more **calcium** from your urine.
    - If that happens, that's going to **reduce the amount of calcium in the urine**.
    - And that's going to be very, very helpful if you have a history of **nephrolithiasis**, right.
- Remember the phrase: **Loops lose calcium, thiazides retain calcium**.
    - So **thiazides** cause **calcium retention**.
    - That can cause you to have **hypocalciuria**, which is **good** if you have nephrolithiasis.
- But again, **loop diuretics** (although we technically don't use them for hypertension) are **not a good idea** if you have a history of **nephrolithiasis**, because loops cause you to **dump more calcium in your urine**.
- If you dump more calcium in your urine, that's going to cause more problems for you.
- It's gonna cause more problems for you.
- Very, very **high-yield** — you have to know this stuff for your exams, right.

Hypertension and Osteoporosis

- And then remember, **thiazides** are also helpful if a person has **osteoporosis**, right.
- If you've got **hypertension** and you have **osteoporosis**, **thiazides** are really good.
- Because again, they **raise your blood calcium levels**.
- So because they raise your blood calcium, they are very, very, very good for helping with **osteoporosis**, right.
- Because they're kind of like **sprucing up your blood calcium**.
- They can **spruce up your blood calcium**.

- And then another weird thing that is actually pretty **high-yield** to know with **thiazide diuretics** is that our friends at the **NBME** can ask you about…
- If a person has been on a **thiazide therapy** for a few weeks, which of the following will be expected with your **parathyroid hormone (PTH)** response?
- Well, I really hope you're saying that the **endogenous PTH should fall**.
- Why? Because again, you're literally **raising the blood calcium levels**.
- You're literally **raising the blood calcium levels**, right.

- And then don't forget that your **thiazide diuretics** also have a few more problems with them.
- The thing is, thiazides are one of these classic things…
- When people say, "Oh, Step 2, Step 3, they're testing a bunch of **basic sciences**," thiazide diuretics are like very classic fodder for that, right?

Thiazides & Blood Glucose

- So remember **thiazide diuretics**?
- They can give you a question about a person that has a history of **diabetes**, and the person was placed on a **thiazide diuretic** for their **hypertension**.
- And then they noticed that for the next few weeks after their therapy has been started, their **blood glucose** has been more elevated than normal.
- If you see something like this, our friends at the NBME can ask you about the **mechanism** behind it.
- And you want to pick the answer that talks about some kind of **drug interaction**.

- So why is it that thiazides mess up your blood glucose control if you're a diabetic?
- The thing is, **thiazides** — we know that they work at the **distal convoluted tubule**.
- They inhibit that **sodium-chloride symporter** that causes you to reabsorb sodium and chloride at the distal convoluted tubule, right.
- But the thing is, **thiazides** also have this **secondary mechanism of action**.
- They can actually **open up potassium channels**.
- When you open up potassium channels, that's actually kind of beneficial because you can get a **vasodilatory effect** from thiazide diuretics.

- But can you think of any other part of your body that contains **potassium channels**?
- Anything kind of linked with **insulin**?
- I would hope you think about those **beta cells** in the **islets of Langerhans**, right.
- Remember, for them to secrete **insulin**, the following process happens:
    - Potassium channels are going to **close** under the action of **ATP**.
    - ATP closes those channels.
    - When those channels close, potassium cannot leak out anymore.
    - The cell depolarizes.
    - Voltage-gated calcium channels open.
    - **Calcium comes in → insulin is secreted**.
- So that’s how the insulin secretion process works.

- But thiazides can **open potassium channels**.
- If you open up that potassium channel with a **thiazide diuretic**, the beta cell is not going to depolarize.
- Those **voltage-gated calcium channels** are not going to open.
- If they don't open, then you're not going to see **insulin secretion**.
- Result:
    - Poor blood glucose control.
    - Impaired insulin response.
- That's why thiazide diuretics can cause **hyperglycemia** — they can **raise your blood glucose levels** because they **suppress insulin production**.

Thiazides & Gout

- And then remember, **thiazides** are also not the greatest if you have a history of **gout**.
- Why?
    - Because they compete for the same transporters used to **excrete uric acid** in the kidneys.
    - If you have decreased excretion of uric acid, then your **serum uric acid levels** go up.
    - That can put you in trouble with **gout**, right.
- So they can give you a question where:
    - A patient is started on an **antihypertensive**.
    - And a few weeks later, the patient presents with **acute severe joint pain**.
    - That acute severe joint pain is **gout**, right.

Thiazides & Gout

- And then they can ask you about the **mechanism** behind the person's **gout**.
- It's going to be from **hyperuricemia**, right.
- More specifically, it's going to be from **decreased uric acid excretion**.
- Again, the thing is, on the **USMLEs** these days — and this is something I elaborate on in many of my classes — the USMLEs, they test **mechanisms, mechanisms, mechanisms**, right.
- It's one of the more effective ways to combat blind memorization, right?
- It's honestly pretty genius.
- Just like, hey, why put the actual disease or straight-up answer that people are familiar with when I can just put a **mechanism answer** instead, right.
- So that's something that they do all the time these days on the exams.
- So again, this is one of these **mechanisms** that is very helpful.

Thiazide Side Effects (Mnemonic HyperGLUC)

- So we've kind of italicized from the perspective of **hyperglycemia**.
- We've talked about how they cause **hyperuricemia**.
- Again, they cause you to increase the **reabsorption of calcium** from your urine, right?
- So they cause **hypercalcemia**, which again is beneficial if you have a history of **nephrolithiasis**.
- And then you heard me say **HyperGLUC**, right?
- So the **L** — what does the **L** stand for?
- The L stands for **hyperlipidemia**, right?
- So **thiazides** can cause **hyperlipidemia**.
- How can they cause hyperlipidemia?
    - Again, it's from that same **insulin effect**.
    - They **suppress insulin production**.
    - Remember, one of the things that insulin does is that it causes you to put more **lipids inside adipocytes**, right?
    - So if you're not making insulin, you won't put lipids inside your adipocytes.
    - So your **serum lipid levels** are going to rise, right.
    - Your serum lipid levels are going to rise, right.
- Again, that's pretty **high-yield** to know for your exams.

- All right, so I think I've hit **thiazide diuretics** strongly enough.
- So let's go into two or three other concepts that I want to review.
- And then we'll go ahead and wrap this rapid review up.
- Again, please — all these things I'm talking about, you may think that they will never show up on your exams until they **show up on your exams**.

HIV & Nephrotic Syndrome

- All right, so now let's talk about what if they give you a question about a person and they tell you that this person is **HIV positive**.
- And this **HIV patient** comes to the physician's office because he has noticed **bilateral leg swelling**, right.
- And then they tell you that on physical exam he has like **3+ pitting edema** of the bilateral lower extremities, right.
- And then they provide a **urinalysis**, and they tell you that this person has like **5+ proteinuria**.
- But then they also tell you that this person has a lot of **oval fat bodies / lipid structures** in the urine.
- And then they ask you: which of the following is the **underlying mechanism** behind those **lipid casts** that we find in this person's urine?

Breaking It Down

- Let's unpack this question.
- This stuff is actually pretty **high-yield** to know for your exams.

1. **Integration**: Do not ignore integrations on your exams.
    - Do not, do not ignore integrations on your exams.
2. **Diagnosis**: What does this patient have?
    - This patient has a **nephrotic syndrome**.
    - What kind? I would hope you're saying **FSGS** (*focal segmental glomerulosclerosis*).
    - Remember, this is the **most common cause of nephrotic syndrome** in people that have **HIV**.
3. **Prognosis**: What is the most likely outcome of this person's nephrotic syndrome?
    - Think **chronic renal failure**.
    - Remember, more than **50% of people with FSGS** will progress to **end-stage renal disease**.
    - FSGS has one of the **worst prognoses** among nephrotic syndromes.
4. **Subtype in HIV**: What is the likely subtype of FSGS in HIV patients?
    - It’s going to be the **collapsing FSGS**.
    - Collapsing FSGS is one of the **worst prognosis subtypes**, and it is classically associated with **HIV**.

Lipid Casts

- So obviously the presentation makes sense — it's a **nephrotic syndrome**.
- But the exam may ask: **what's the mechanism behind the lipid casts?**
- Here's the thing: the **USMLE** loves mechanism-style questions.
- When they do **pool changes**, students often freak out about "pool change, pool change."
- But when the USMLE does pool changes, two things happen:
    1. They bring in a few new concepts (maybe ~10% of the exam).
    2. They **repurpose old concepts** and just **test them in new ways**.
- I'm telling you this: if you really set your mind to it, you can actually create **multiple concepts from the same concept**, right?
- Like, for example, I bet many of you have never heard of what I'm about to describe.
- It's like, why is it that there are **lipid casts** in a person that has a **nephrotic syndrome**?
- Well, let me break it down for you guys, right?

Mechanism of Lipid Casts in Nephrotic Syndrome

- So here's the thing that happens:
    - We know that when you lose all this **protein** in your urine in **nephrotic syndrome**, you're going to have a reduction in the **oncotic pressure** in your bloodstream.
    - When you have that reduction in oncotic pressure, right, that's going to cause you to have a lot of **fluid extravasation**.
    - You're going to have a lot of **edema**.
- So your body is like, "Man, I keep losing all this protein. I gotta figure out a way to help my oncotic pressure issue."
- So how does your body fix that problem?
    - One of the ways it fixes that problem is by your **liver generating a ton of lipid**.
    - Because at least **lipids** can exert some oncotic/osmotic pressure in your bloodstream.
- But the thing is, because you're now making so many excess lipids, some of those lipids can also begin to **leak out into your urine**.
- That's the **mechanism behind lipid casts** in the urine when people have **nephrotic syndrome**.
- In fact, you may notice sometimes on the **USMLE exams**, instead of calling it **nephrotic syndrome**, they may call it **lipoid nephrosis**.
- **Lipoid nephrosis, lipoid nephrosis.**
- All right, that's the **mechanism behind the lipid casts** we find in the urine in people that have nephrotic syndrome.